Remarks

Further and favorable reconsideration is respectfully requested in view of the foregoing amendments and following remarks.

Initially, the Office Action Summary page fails to acknowledge that claims 41-51 are also pending in the application, although these claims have been withdrawn from further consideration as being directed to non-elected subject matter.

Claim 10 has been amended to require that component v is a mixture of at least two non-ionic surfactants taken from those recited in claim 37. Accordingly, claim 19 has been amended to require a mixture of the surfactants.

Claim 22 has been amended to depend on claim 11, in order to provide proper antecedent basis for the flavor enhancing agent.

Claim 24 has been amended to require that component i is a combination of water-soluble polymers, which in addition to the water-soluble cellulose derivatives, further comprises one or more water-soluble polymers which are recited in claim 43.

Claim 35 has been amended to depend on claim 34, in order to provide proper antecedent basis for the polyalcohol.

The patentability of the presently claimed invention over the disclosures of the references relied upon by the Examiner in rejecting the claims will be apparent upon consideration of the following remarks.

Thus, the rejection of claims 10-11, 18-24 and 26-27 under 35 U.S.C. §103(a) as being unpatentable over Roreger et al. (US '745) is respectfully traversed.

The only independent claims subject to this rejection are claims 10 and 24. Claim 10 has been amended, as indicated above, to require a mixture of at least two non-ionic surfactants, the mixture comprising a first component which is a polyoxyethylene sorbitan fatty acid ester or a α-hydroxy-ω-hydroxypoly(oxyethylene)poly(oxypropylene)poly(oxyethylene) block copolymer, and a second component which is a polyoxyethylene alkyl ether or a polyoxyethylene castor oil derivative. Applicants take the position that the Roreger et al. reference does not suggest a monolayer film formed from a mucoadhesive composition which comprises a mixture of two non-ionic surfactants as now defined in claim 10.

Furthermore, as regards the surfactants, the Examiner states that surfactants "such as glycerol diacetate, which is a surfactant" may be included in the film, and that the combination

of a softener (glycerol diacetate; Roreger et al., column 4, lines 1-2) and a surfactant may be considered two surfactants. However, substances such as glycerol diacetate are generally regarded as softeners but not as surfactants, and the Examiner's statement "glycerol diacetate, which is a surfactant" is considered to be incorrect.

Therefore, the subject matter of independent claim 10 is not obvious from Roreger et al., and the same applies to dependent claims 11 and 18-23.

Claim 24 has been amended, as indicated above, to require a combination of water-soluble polymers, the combination comprising one or more substances selected from the group consisting of water-soluble cellulose derivatives and further comprising one or more water-soluble polymers selected from the group consisting of polyvinyl pyrrolidone, carboxymethyl cellulose, polyvinyl alcohol, sodium alginate, polyethylene glycol, natural gums, water-dispersible polyacrylates and carboxyvinyl copolymers.

Also with respect to claim 24, Applicants point out that this claim is drawn to a monolayer film containing **nicotine** or nicotine salt as pharmaceutically active substance (component (ii)), in combination with menthol or mint flavor, aspartame or sorbitol, and tartaric acid (components (iii), (iv) and (v)).

While it is true that Roreger et al., in column 11, lines 20-21, also mention "nicotine" as an example of a systemic active substance, it is important to note that this reference teaches that nicotine is an insecticide (column 11, line 22) which may be incorporated into a gel film which is intended to be used for the treatment of plants, in order to protect them against agents of diseases or parasites (column 11, lines 5-19). The nicotine-containing gel film as taught by Roreger et al. is applied to the surface of a plant or wrapped around parts of the plant (column 11, lines 5-8, 15-19, and 25-28).

In this regard, the Examiner refers to the disclosure at column 10, lines 31-35 of Roreger et al. for a disclosure of hydrophilic gel films that may be used to deliver active substances via the mucous membrane. The Examiner then refers to column 11, lines 20-22 for systemic actives such as nicotine. But the first disclosure cited by the Examiner, i.e. column 10, lines 31-35, is for a completely different embodiment of Roreger et al. than the embodiment at column 11, lines 20-22, i.e. application of the gel film to mucous membranes is completely unrelated to application of the gel film to the surface of a plant. If one skilled in the art were to prepare a gel film for application to a mucous membrane, he/she would certainly not incorporate an insecticide

in the gel film. Roreger et al. specifically refer to nicotine as an insecticide, which would be appropriate for a gel film applied to the surface of a plant. But the art-skilled would not obtain any suggestion in Roreger et al. which would lead them to incorporate nicotine in the gel film for application to a mucous membrane. Considering that mucosal tissue (as recited in present claim 24) is fundamentally different from the plant surfaces mentioned by Roreger et al., the nicotine-containing film described in column 11 of the reference cannot be expected to be "able to be adhered to an oral cavity and immediately softens after application to mucosal tissue", as recited in claim 24.

In addition, since Roreger et al. only consider the use of nicotine as an insecticide for the treatment of plants, the incorporation of flavoring agents, sweeteners and flavor enhancing agent (as presently claimed) cannot be regarded as being obvious in view of the reference teaching. While Roreger et al. also mention the possible use of essential oils such as peppermint oil or menthol (column 12, lines 1-3), these substances are intended for the treatment of colds (column 11, lines 62-63), and there is no apparent reason why one skilled in the art would combine a device for the treatment of plants (containing nicotine, as discussed above) with a device for the treatment of colds (containing flavoring agents such as peppermint oil or menthol) which is intended for human patients.

Therefore, the monolayer film of present claim 24 is not rendered obvious by the teaching of Roreger et al., and the same applies to dependent claims 26 and 27.

The rejection of claims 12-17 and 25 under 35 U.S.C. §103(a) as being unpatentable over Roreger et al. in view of Inoue et al. (US '470) is respectfully traversed.

The comments set forth above concerning the Roreger et al. reference are equally applicable to this rejection.

The Examiner cites the Inoue et al. reference for disclosing film thickness or the presence of a coloring agent. Since claims 12-17 and 25 are dependent on independent claims 10 and 24, respectively, the above arguments also support the patentability of these claims. With respect to independent claims 10 and 24, it is noted that Inoue et al. neither suggests the incorporation of a mixture of nonionic surfactants as defined in claim 10 as now amended, nor the use of nicotine as a pharmaceutically active substance that can be administered via a mucosal surface.

The Examiner states that "the reference (Inoue et al.) differs from the instant claims insofar as it does not disclose nicotine in the compositions". Since Roreger et al. merely suggest

nicotine as an insecticide for the treatment of plants, and since Inoue et al. does not mention nicotine at all, the inclusion of this active substance in the monolayer film of the present claims could not even be considered obvious if both references were combined.

The rejection of claims 28-29, 31, 33-35, 38-40 and 53-56 under 35 U.S.C. §103(a) as being unpatentable over Keith et al. (US '378) in view of Lovgren et al. (US '505) and Inoue et al. is respectfully traversed.

The only independent claim among these claims is claim 28, which is directed to a film-shaped composition which contains the active substance, nicotine, and further comprises polyvinyl pyrrolidone (PVP) and hydroxypropylmethyl cellulose (HPMC), and which can be applied to the oral cavity for releasing this active substance to the oral cavity.

As noted by the Examiner, the primary reference (Keith et al.) differs from the instant claims in that the prior art films do not comprise hydroxypropylmethyl cellulose, and in that the films are not described as having a thickness of 70 μm or less. With respect to HPMC, the Examiner has cited Lovgren et al. as a secondary reference which is used as a general teaching that discloses HPMC and PVP are used for rapidly disintegrating compositions. However, Applicants submit that the proposed combination of teachings is inappropriate and, therefore, cannot properly be used to support a rejection for obviousness.

The Lovgren et al. reference relates to enteric coated dosage forms of omeprazole. These dosage forms are provided with an enteric coating which protects the dosage form from becoming dissolved before it arrives in the small intestine. This is necessary in order to protect this particular active substance, omeprazole, against unwanted degradation in the acidic environment of the stomach (gastric juice; see Lovgren et al., column 1, lines 6-11 and 30-39; and column 3, lines 14-33). HPMC is mentioned by Lovgren et al. as a component of a "separating layer" which is applied as an intermediate layer between the inner tablet core which contains the active substance, and the outer enteric coating. This "separating layer" is necessary to avoid possible contact between the active substance, omeprazole, and the enteric coating polymers which contain free carboxyl groups and which may, therefore, cause degradation of omeprazole during manufacture or storage (see column 4, lines 4-8 and 31-45).

From the above, it follows that according to Lovgren et al., the incorporation of HPMC (and PVP) is necessitated by using omeprazole as the active substance, and by providing the dosage forms with an enteric coating. It also follows from Lovgren et al. that the dosage forms

described in this reference are certainly not capable of releasing an active substance in the oral cavity, since these dosage forms are specifically constructed to ensure that omeprazole is only released in the intestine. It is also pointed out that Lovgren et al. is not concerned with "thin films" (max. 70 μm) but rather with tablets comprising a core and an outer coating (see Examples).

Since neither Keith et al. nor the presently claimed invention (claim 28) relates to dosage forms for releasing active substances in the intestine, and since the dosage forms described by Lovgren et al., due to the presence of an enteric coating, are not capable of releasing the active substance in the oral cavity, **the teaching of Lovgren et al. is incompatible with the teaching of Keith et al.** and, therefore, a person of ordinary skill in the art would not consider the possibility of combining such conflicting teachings.

In this connection, it is also pointed out that the Examiner's statement (page 6, lines 14-16) that Lovgren et al. discloses HPMC and PVP are used for rapidly disintegrating compositions is incorrect. **The oral dosage forms of Lovgren et al. are most certainly not "rapidly disintegrating"** since they are protected against premature disintegration by an enteric coating layer which ensures that the oral dosage forms, after having been ingested, reach the small intestine without degradation (column 1, lines 35-39). This clearly indicates that disintegration is retarded rather than "rapid".

HPMC and PVP are taught by Lovgren et al. only in connection with the "separating layer", and the incorporation of this separating layer is only necessary to prevent possible interactions between the active substance and the polymers of the enteric coating, as discussed above. Therefore, when there is no enteric coating, the need for adding a separating layer is also obviated. Since the buccal dosage forms of Keith et al. do not comprise any enteric coatings, there would have been no motivation to add a separating layer as taught by Lovgren et al. Therefore, **Lovgren et al. does not suggest adding HPMC to the buccal dosage forms of Keith et al.** which are essentially based on polyethylene glycols, polyethylene oxides and PVP.

On page 7 of the Office Action (last paragraph), the Examiner concluded that it would have been obvious to have used HPMC as a high molecular weight polymer in the compositions of the primary reference motivated by the desire to use a polymer that will not impede the dissolution of the film when placed in the mouth. However, apart from the above argument that Keith et al. and Lovgren et al. cannot be combined as they concern conflicting teachings,

Applicants submit that the absence of a certain property ("will not impede the dissolution") in a component (HPMC) cannot be regarded as a positive motivation for incorporating this component into a composition disclosed in a prior art reference.

Inoue et al. appears to have been cited only for teaching the thickness of the film and addition of flavoring and coloring agents. However, on page 7 of the Office Action, it is stated that this reference differs from the instant claims (only) insofar as it does not disclose nicotine in the compositions. This is not correct, since Inoue et al. also fails to disclose the combination of PVP and HPMC recited in present claim 28. The compositions of Inoue et al. are based on polycarboxylic acids and polyvinyl acetate (column 6, lines 1-5). In addition, the oral bandages of Inoue et al. are described as being adapted for the delivery of topical drugs (see the Abstract; and column 9, lines 3-53). In contrast, **nicotine is not a topical drug**, but a drug producing **systemic** effects. As was noted by the Examiner, Keith et al. consider using nicotine as an active substance. However, the buccal dosage forms of Keith et al. are based on polyethylene glycol and PVP, rather than PVP and HPMC.

The rejection of claims 30 and 52 under 35 U.S.C. §103(a) as being unpatentable over Keith et al. in view of Lovgren et al. and Inoue et al. and further in view of Stanley et al. (US '207) is respectfully traversed.

The comments set forth above concerning the primary reference and both secondary references are equally applicable to this rejection.

The Examiner applies the Stanley et al. reference for a teaching of using nicotine salts. However, since claims 30 and 52 are directly or indirectly dependent on claim 28, and since claim 28 is patentable over Keith et al. and both secondary references for the reasons set forth above, Applicants submit that the subject matter of claims 30 and 52 is also patentable over the same references taken with Stanley et al.

The rejection of claims 36 and 37 under 35 U.S.C. §103(a) as being unpatentable over Keith et al. in view Lovgren et al. and Inoue et al. and further in view of Story et al. (US '949) is respectfully traversed.

Claims 36 and 37 are both dependent on claim 28, which is patentable over the primary reference and both secondary references for the reasons set forth above.

The Examiner has admitted that Keith et al., Lovgren et al. and Inoue et al. fail to disclose incorporating surfactants into oral compositions, and Story et al. was cited "as a general

teaching to disclose surfactants are used to dissolve drugs". However, it is evident from the description of Story et al.'s invention that this teaching is not to be taken as a "general" teaching. The teaching of Story et al. relates to a specific (or exceptional) case where **specific** types of surfactants are used to form micelles when combined with a **specific** class of drugs (non-steroidal anti-inflammatory drugs; see the Abstract and claim 1). The resulting micelles are lipid-coated **vesicles** (column 5, lines 7-16), and they are incorporated into **capsules or solutions** (see Examples). However, Story et al. do not refer to a film as recited in claim 28. Therefore, it remains speculative whether the micelles/vesicles could be incorporated into a film without impairing the structure of the film.

On page 9 of the Office Action it is stated that the surfactant is used to dissolve the drug in Story et al.'s teaching. But this is incorrect, since this reference teaches that the surfactant is used for **forming micelles** which contain the drug (see column 4, lines 33-38), and "forming micelles" is not indicative of "dissolving" the drug. Nothing in Story et al.'s teaching suggests that the surfactants could be used "to ensure the drug was thoroughly dissolved and made a uniform mixture throughout the film", as indicated by the Examiner on page 10 of the Office Action. Rather, the surfactants are used for micelle formation according to Story et al.

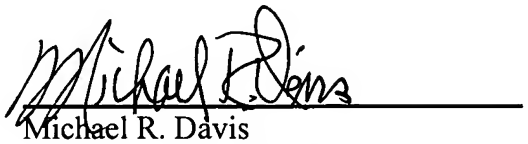
Furthermore, Story et al. relate to dosage forms (capsules and solutions) that are fundamentally different from the dosage forms of the present invention and the primary reference (thin films). Therefore, a skilled person could not have known whether micelle formation would be compatible with thin polymer films, and would not have been motivated to combine Story et al.'s teaching with the other cited references due to these fundamental differences. In addition, the dosage forms described by Story et al. are not intended for releasing active substances in the oral cavity (see column 4, lines 18-20).

For these reasons, Applicants take the position that the presently claimed invention is clearly patentable over the applied references.

Therefore, in view of the foregoing amendments and remarks, it is submitted that each of the grounds of rejection set forth by the Examiner has been overcome, and that the application is in condition for allowance. Such allowance is solicited.

Respectfully submitted,

Horst Georg ZERBE et al.

By: 

Michael R. Davis
Registration No. 25,134
Attorney for Applicants

MRD/pth
Washington, D.C. 20006-1021
Telephone (202) 721-8200
Facsimile (202) 721-8250
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